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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/823,980	03/25/97	WEINER	A CHIR-0108

EXAMINER	
SCHWADRON, R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commiaaioner of Patenta and Trademarka

Office Action Summary	Application No. 08/823,980	Applicant(s) Weiner et al.
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

☐ Responsive to communication(s) filed on _____.

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *40-53* is/are pending in the application.

Of the above, claim(s) *43, 44, 46, 47, 50, and 51* is/are withdrawn from consideration.

☐ Claim(s) _____ is/ere ellowed.

☒ Claim(s) *40-42, 45, 48, 49, 52, and 53* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Claims 40-42,45,48,49,52,53 are under consideration.

RESPONSE TO APPLICANTS ARGUMENTS

2. The amendment filed 2/1/99 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows.

The new matter is SEQ. ID. No. 8 wherein said sequence recites Xaa at a variety of positions in said sequence wherein said sequence encompasses any sequence with any combination of amino acids specified by the Xaa amino acids as defined in the sequence listing. There is no disclosure of SEQ. ID. No. 8 in pages 1-43 of the specification or the claims as originally filed. Figure 2-1 of the specification discloses the HCV E2HV sequences for 90 HCV isolates (see Brief description of drawings and specification, Example 1). Example 1 discloses that Figure 2 shows a conserved motif from 90 E2HV isolates. This motif is listed as the first line of Figure 2-1 as ".T.VTGG.AARTT.G..SLF..G.SQ.IQLI". Figure 2 seems to possibly indicate that "." as recited in said sequence refers to a variety of different amino acids that were found in said sequence at the position listed in the 90 sequences actually disclosed in Figure 2. However, the consensus sequence also seems to specifically refer to the 90 sequences disclosed in Figure 2 and not encompass permutations wherein "." at the first position is the amino acid disclosed in sequence 2, while "." third position is derived from sequence 5, etc. The consensus sequence simply discloses that of the 90 sequences disclosed in Figure 2, that most of said sequences had a pattern of amino acids generally similar to that in the consensus sequence. The specification does not disclose the consensus sequence recited in Figure 2 wherein "." represents any Xaa amino acid as specified in the sequence listing in combination with any other Xaa amino acid specified in the sequence listing. It is equally unclear if "." as recited in the consensus sequence actually even had a contemplated amino acid at said position or whether "." simply designated a portion of the

sequence that was generally more variable than other portions of the consensus sequence which were assigned a particular amino acid.

Applicant is required to cancel the new matter in the reply to this Office action.

Applicants arguments in the amendment filed 9/28/98 have not addressed the issues raised in this rejection.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 40-42,45,48,49,52,53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "Xaa-Thr-Xaa-Val-Thr-Gly-Gly-Xaa-Ala-Ala-Arg-Thr-Thr-Xaa-Gly-Xaa-Xaa-Ser-Leu-Phe-Xaa-Xaa-Gly-Xaa-Ser-Gln-Xaa-Ile-Gln-Leu-Ile (SEQ. ID NO:8)" in claim 40. There is no disclosure of SEQ. ID. No. 8 in pages 1-43 of the specification or the claims as originally filed. Figure 2-1 of the specification discloses the HCV E2HV sequences for 90 HCV isolates (see Brief description of drawings and specification, Example 1). Example 1 discloses that Figure 2 shows a conserved motif from 90 E2HV isolates. This motif is listed as the first line of Figure 2-1 as ".T.VTGG.AARTT.G..SLF..G.SQ.IQLI". Figure 2 seems to possibly indicate that "." as recited in said sequence refers to a variety of different amino acids that were found in said sequence at the position listed in the 90 sequences actually disclosed in Figure 2. However, the consensus sequence also seems to specifically refer to the 90 sequences disclosed in Figure 2 and not encompass permutations wherein "." at the first position is the amino acid disclosed in sequence 2, while "." third position is derived from sequence 5, etc. The consensus sequence simply discloses that of the 90 sequences disclosed in Figure 2, that most of said sequences had a pattern of amino acids generally similar to that in the consensus sequence. The specification does not

disclose the consensus sequence recited in Figure 2 wherein "." represents any Xaa amino acid as specified in the sequence listing in combination with any other Xaa amino acid specified in the sequence listing. It is equally unclear if "." as recited in the consensus sequence actually even had a contemplated amino acid at said position or whether "." simply designated a portion of the sequence that was generally more variable than other portions of the consensus sequence which were assigned a particular amino acid. There is no written description in the specification as originally filed of the claimed invention (eg. it constitutes new matter).

Applicants arguments in the amendment filed 9/28/98 have not addressed the issues raised in this rejection.

5. Claims 40-42,45,48,49,52,53 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reason elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification as originally filed for the recitation of "wherein the amino acid sequence motif is the only sequence corresponding to a hypervariable domain of hepatitis C virus" in the context recited in claim 40. There is no written description in the specification as originally filed of the claimed invention (eg. it constitutes new matter).

Regarding applicants comments in the amendment filed 9/28/98, while the specification defines the E2 hypervariable region as amino acids 384-414, there is no disclosure in the specification of the claimed invention which is a polypeptide comprising the amino sequence recited in the claims "wherein the amino acid sequence motif is the only sequence corresponding to a hypervariable domain of hepatitis C virus". Applicant has not pointed out support for the claimed invention in the specification or claims as originally filed.

6. Claims 40-42,45,48,49,52,53 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

The specification is not enabling for the claimed peptides wherein the peptides are "immunogenic". The claims recite that the peptide recited in the claims is immunogenic. The claims under consideration encompass a vast number of different peptides because of the recitation of Xaa in various portions of the formula used to depict the claimed peptide. There is no disclosure in the specification as to which of the vast number of peptides encompassed by the claimed peptide are immunogenic and which are not. The claims under consideration do not specifically read on naturally occurring peptides that are found in HCV. The claims under consideration encompass peptides that are not found in HCV. In fact, the peptide of claim 40 and 53 is not found in nature (eg. it represents a "consensus" peptide based on frequently occurring amino acids found in 90 sequenced HCV isolates, while said sequence is not actually found in any of the sequenced isolates). There is no evidence of record that such a peptide exists in nature. It would require undue experimentation to determine which of the vast numbers of peptides encompassed by the claims under consideration are immunogenic and which are not. Regarding the peptide disclosed in Example 2 in the specification, said peptide is not encompassed by the claimed peptide (eg. it differs in amino acid sequence from the claimed peptide). The art recognizes that antibodies bind to a particular three dimensional epitope formed by a particular peptide epitope (see Berzofsky page 176, second column, continued on page 177). There is no disclosure in the specification that the sequence recited in claim 40 contains an immunogenic epitope which does not have a Xaa inserted in the middle of said epitope. In fact, there is no disclosure in the specification of the nature of actual immunogenic epitopes contained in the claimed peptide. The specification discloses in Example 2 that the peptide of SEQ. ID. No. 2 contains three different potential epitopes bound by antibodies. However, none of these epitopes are found in the claimed molecule. Thus, there is no evidence of record that the claimed invention actually contains immunogenic epitopes. Even if the claimed invention included naturally occurring HCV sequences (which it does not), Weiner et al. (1992) establish that not all naturally occurring HCV E2/NS1 derived peptides are immunogenic (see paragraph 18 of the Office action mailed 7/24/96). However, the claimed invention is limited to nonnaturally occurring HCV derived peptides because the amino acid motif recited in the claim encompasses a vast number of peptides wherein said peptides are not found in HCV. The art recognizes that antibodies bind to a particular three dimensional epitope formed by a particular peptide epitope (see Berzofsky page 176, second column, continued on page 177). The claims under consideration encompass

nonnaturally occurring peptides which may or may not possess an immunogenic epitope because said peptides do not possess a three dimensional peptide epitope similar to that occurring in a naturally occurring HCV peptide. It would require undue experimentation determine what peptides encompassed by the claimed invention are immunogenic and which peptides were not.

Regarding applicants comments, the claimed invention encompasses vast numbers of peptides wherein the peptides are not restricted to naturally occurring HCV E2/NS1 epitopes. It would require undue experimentation to determine what peptides encompassed by the claimed invention are immunogenic and which peptides were not. The art recognizes that antibodies bind to a particular three dimensional epitope formed by a particular peptide epitope (see Berzofsky page 176, second column, continued on page 177). There is no disclosure in the specification that the sequence recited in claim 40 contains an immunogenic epitope which does not have a Xaa inserted in the middle of said epitope. In fact, there is no disclosure in the specification of the nature of actual immunogenic epitopes contained in the claimed peptide. The specification discloses in Example 2 that the peptide of SEQ. ID. No. 2 contains three different potential epitopes bound by antibodies. However, none of these epitopes are found in the claimed molecule. Thus, there is no evidence of record that the claimed invention actually contains immunogenic epitopes. Even if the claimed invention included naturally occurring HCV sequences (which it does not), Weiner et al. (1992) establish that not all naturally occurring HCV E2/NS1 derived peptides are immunogenic (see paragraph 18 of the Office action mailed 7/24/96). However, the claimed invention is limited to nonnaturally occurring HCV derived peptides because the amino acid motif recited in the claim encompasses a vast number of peptides wherein said peptides are not found in HCV. The art recognizes that antibodies bind to a particular three dimensional epitope formed by a particular peptide epitope (see Berzofsky page 176, second column, continued on page 177). The claims under consideration encompass nonnaturally occurring peptides which may or may not possess an immunogenic epitope because said peptides do not possess a three dimensional peptide epitope similar to that occurring in a naturally occurring HCV peptide.

Regarding the Weiner declaration filed 9/28/98, the following comments are made. The Chien et al. and Hattori et al. publications as referred to in the Weiner declaration refer to experiments performed with a single peptide derived from a single actual HCV strain. Said peptide (as disclosed in paragraph 5 of the Weiner declaration) is not encompassed by the formula recited in the claimed invention. Therefore, the experiments referred to in the Weiner declaration are not

relevant to the claimed invention because they were not performed using the peptide of the claimed invention. In addition, the claimed peptides encompass vast numbers of peptides wherein the vast majority of said peptides are not derived from HCV strains and said peptides do not exist in nature. The scope of the evidence supplied in the Weiner declaration is not commensurate with the scope of the claimed invention. Furthermore, there is also no evidence of record that the results disclosed in the Chien et al. publication do not occur because the detected strains have identical amino acid sequences at a particular epitope found in said sequence. The peptide used in said experiments also seems to be derived from a naturally occurring HCV sequence while the peptides recited in the claimed invention encompass sequences that do not occur in HCV.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644
April 7, 1999